

Award Number: W81XWH-07-1-0682

TITLE: Emergency Preservation and Resuscitation for Cardiac Arrest from Trauma (EPR-CAT)

PRINCIPAL INVESTIGATOR:

Dr. Patrick Kochanek, Principal Investigator

CONTRACTING ORGANIZATION:

University of Pittsburgh
Pittsburgh, PA 15213-2303

REPORT DATE: December 2016

TYPE OF REPORT: Addendum to Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) December 2016		2. REPORT TYPE Addendum to Final		3. DATES COVERED (From - To) 26Sep2015 - 25Sep2016	
4. TITLE AND SUBTITLE Emergency Preservation and Resuscitation for Cardiac Arrest From Trauma				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-07-1-0682	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Patrick Kochanek, MD (Principal investigator) Samuel A. Tisherman, MD (Co-investigator) email: kochanekpm@ccm.upmc.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Pittsburgh Office of Research 123 University Place Pittsburgh, PA 15213-2303				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, MD 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT During this eighth year of the project, we completed the community consultation and public disclosure process in Baltimore. The results were submitted to the University or Maryland IRB, which has approved the trial. This approval included changing the local principal investigator to Dr. Tisherman with agreement from the Conflict of Interest Officer. We have also shifted the coordinating center for the study to the University of Maryland. Appropriate documents were subsequently submitted to the US Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO), which has also approved the study. Training for the trauma surgeons involved in the project has been completed. The Shock Trauma Center of the University of Maryland Medical Center is now open for enrollment.					
15. SUBJECT TERMS Trauma, hemorrhagic shock, cardiac arrest, cardiopulmonary resuscitation, hypothermia					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 6	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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Introduction

Cardiopulmonary resuscitation (CPR) can save victims of normovolemic cardiac arrest (CA), e.g., ventricular fibrillation. During exsanguination CA from trauma, however, CPR, even with an emergency department (ED) thoracotomy and open chest CPR, results in unacceptably low survival rates. *Emergency Preservation and Resuscitation (EPR)* was developed to rapidly preserve the organism during ischemia, using hypothermia, drugs, and fluids, to “buy time” for transport and resuscitative surgery. The purpose of this study is to test the feasibility of rapidly inducing profound hypothermia ($\leq 10^{\circ}\text{C}$) with an aortic flush in trauma victims that have suffered CA and failed standard resuscitative efforts to enable resuscitative surgery and delayed resuscitation with cardiopulmonary bypass. The primary outcome variable will be survival to hospital discharge with minimal neurologic dysfunction.

Body

Scientific Progress

In December, 2009, we conducted the first meeting of the Data and Safety Monitoring Board. The group approved moving forward with the study. They recommended standardization of the transfusion protocols across sites, elimination of blunt trauma victims, and the use of Seldinger technique for aortic cannulation. In subsequent meetings, they have also asked for more prolonged follow-up of subjects (to 12 months), including additional functional outcome using the SF-36 form. They further recommended that the trauma surgeons involved in the study obtain hospital privileges for cannulation for the EPR flush. This has been accomplished.

Given the complexity of our planned intervention for trauma patients in cardiac arrest, we need to optimize subject inclusion and exclusion criteria. The literature on such patients is scant, with studies focusing on mortality rates and crude information such as signs of life (pulse, breathing, spontaneous movements) in the field or emergency department and admission cardiac rhythm. To better define this patient population to optimize subject selection, we have initiated a retrospective study to look at other factors that could be quickly determined during the resuscitation of a trauma patient in the emergency department. This retrospective study should produce publishable data, although so far we have not obtained sufficient data from the University of Pittsburgh to make any conclusions. We have initiated a similar study at the University of Maryland.

Separately, to better profile patients who die from trauma, Dr. Tisherman led a study of the hemorrhagic shock database of the Resuscitation Outcomes Consortium, which studies prehospital care in patients with life-threatening injuries. Within this database, we have identified 67 patients with hemorrhagic shock and no significant head injury who died within 24 hours of their injuries. These patients represented 83% of all deaths in the shock cohort. The primary cause of these early deaths was indeed hemorrhage. Twenty-six patients died in the Emergency Department. Data on timing of pulselessness and use of ED thoracotomies is not available in the database. Presumably, many of these patients could have been EPR candidates. Overall, this dataset suggests that the great majority of deaths from traumatic hemorrhage occur within 24 hrs from direct effects of hemorrhage. Late deaths are rare. To improve survival from traumatic hemorrhagic shock, early, novel interventions, such as EPR, are needed.

Administrative and Logistic Matters

The first regulatory step for proceeding with this study was to obtain an Investigational Device Exemption (IDE) from the Food and Drug Administration (FDA). Our trial is complicated by the fact that both fluids and equipment are to be used for an application that is not currently approved by the FDA. We have now obtained an investigator-sponsored IDE from the FDA Center for Devices and Radiological Health Office of Device Evaluation.

With the approval of the IDE, we were able to obtain approval for the proposal from the University of Pittsburgh Institutional Review Board (IRB) as both the coordinating center and participating site. We have now completed the community consultation and public disclosure processes. These included the meetings with the Pittsburgh Human Relations Commission and the University of Pittsburgh Center for Minority Health, a random-digit telephone survey, surveys in trauma clinic, town hall meetings at the University Student Union, a website, and publicity in local and national media. The results were presented to the IRB and IRB approval has been granted. We have also obtained human use approval from the USAMRMC. The Pittsburgh site was open for enrollment between the spring of 2014 and early 2015. Because of staffing changes, the site has been on clinical hold since then.

Similarly, the University of Maryland IRB and the USAMRMC have approved the study. The Shock Trauma Center of the University of Maryland Medical Center is now open for enrollment.

Other centers that have been identified for possible inclusion in the study in the future include the University of Texas – Houston, Oregon Health and Sciences University, and the University of Colorado.

Because Drs. Tisherman and Kochanek are co-authors of a submitted patent for EPR Methods, the Universities of Pittsburgh and Maryland Conflict of Interest Offices have reviewed the plans for the trial and defined a plan to manage the conflict so that these researchers could still be involved in the study.

Key Research Accomplishments

During this past year, the primary accomplishment has been completion of the community consultation and public disclosure process in Baltimore, allowing us to receive approval from the University of Maryland IRB and the USAMRMC. We also completed training of the designated trauma surgeons. This site is now open for enrollment.

Reportable Outcomes

We have not enrolled any patients in the study.

Conclusion

Most of the work so far on this project has been focused on the regulatory and training processes. We have an IDE and full approval from two IRBs. We are ready for enrollment at the Shock Trauma Center of the University of Maryland Medical Center.

References

None